

Jacques E. Gielen, Ph.D.  
Laboratoire de Chimie Medicale  
Unite de Biochimie  
Institut de Pathologie  
Universite de Liege  
B-4000 Sart-Tilman par Liege 1  
Belgique

**Cigarette Smoke and Polycyclic Hydrocarbon Metabolism in Rat and Mouse Lung and Kidney.**

Potent inducers of aryl hydrocarbon hydroxylase are present in cigarette smoke. In rats and mice, they specifically increase the lung and kidney enzymatic activity. Certain biochemical characteristics of this phenomenon make the investigators believe that the responsible inducing substances in the cigarette smoke might be different from the polycyclic hydrocarbons.

The researchers' immediate goals will be (1) to identify those inducers and (2) to further characterize the biochemical mechanism of their action compared to other well-known inducers. Their longer range program includes a detailed biochemical study of the various enzymes (aryl hydrocarbon hydroxylase, epoxyde hydratase, glutathione transferase) involved in the polycyclic hydrocarbon metabolism, as well as a molecular approach of the early biochemical modifications produced in the target tissues (lung and kidney) by the polycyclic hydrocarbons.

Presently, the investigators are studying in more detail the mechanisms of AHH induction by cigarette smoke condensate fractions mainly using different cell lines in culture as models. They are also analyzing the action of cigarette smoke on the activity of other enzymes of polycyclic hydrocarbon metabolism, (epoxyde hydratase and glutathione transferase), as well as on the binding of polycyclic hydrocarbon metabolites to the macromolecules of rat and mice (inducible and non-inducible) lung and kidney.

In the very near future, they will also further analyze the chemical composition of the smoke condensate fractions in relation to their effect on the drug metabolizing enzymes. High pressure liquid chromatography will be used to further separate the components of those fractions. Gas liquid chromatography coupled to the mass spectrometry will be utilized for precise analytical work and identification of the main constituents.

Activation Date: June 1, 1976

Current Grant Level: \$47,000.

1005075441